



PTO/SB/08B (04-07)

Approved for use through 09/30/2007. OMB 0851-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	10/501,628
Filing Date	November 22, 2004
First Named Inventor	Alberto Martin
Art Unit	1636
Examiner Name	Kimberly A. Makar, Ph.D.
Attorney Docket Number	96700/905

Sheet 1 of 1

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
/KM/	1	CUMBERS, S.J. et al., "Generation and iterative affinity maturation of antibodies in vitro using hypermutating B-cell lines"; Nature Biotechnology, 2002, Vol. 20, pp1129-34.	
↓	2	STORB, U. et al., "Somatic hypermutation of immunoglobulin and non-immuoglobulin genes"; Phil. Trans. R. Soc. Lond. B, 2001, Vol. 356, pp. 13-19	
↓	3	WANG, L. et al., "Evolution of new nonantibody proteins via iterative somatic hypermutation"; PNAS, 2004, Vol. 101, No. 48, pp. 16745-49.	

Examiner Signature	/Kimberly Makar/	Date Considered	08/20/2007
-----------------------	------------------	--------------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Complete if Known

(Use as many sheets as necessary)

Sheet	1	of	
-------	---	----	--

Application Number	10/501,628
Filing Date	November 22, 2004
First Named Inventor	Alberto Martin
Art Unit	1636
Examiner Name	Kimberly A Makar, Ph.D.
Attorney Docket Number	96700/905

[illegible][illegible]

Examiner Signature	/Kimberly Makar/	Date Considered	08/20/2007
-----------------------	------------------	--------------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)		Complete if Known	
		Application Number	10/501,628
		Filing Date (I.A. Filing Date)	01/15/2003
		First Named Inventor	Alberto Martin
		Art Unit	to be assigned
		Examiner Name	to be assigned
Sheet	1	of	4
		Attorney Docket Number	96700/905

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
/KM/	1	ARAKAWA H. et al., "Requirement of the Activation-Induced Deaminase (AID) Gene for Immunoglobulin Gene Conversion"; Science, 2002, Vol. 295, pp. 1301-6.	
	2	BACHL J. et al., "Increased transcription levels induce higher mutation rates in a hypermutating cell line"; J. Immunol, 2001, Vol.166, No. 8, pp. 5051-7.	
	3	BEMARK M. et al., "The c-MYC allele that is translocated into the IgH locus undergoes constitutive hypermutation in a Burkitt's lymphoma line"; Oncogene, 2000, Vol. 19, No. 30, pp. 3404-10.	
	4	DAVIDSON N.O. et al., "Apolipoprotein B: mRNA Editing, Lipoprotein Assembly, and Presecretory Degradation"; Annu. Rev. Nutr., 2000, Vol. 20, pp. 169-93.	
	5	GREEN N.S. et al., "Immunoglobulin hypermutation in cultured cells"; Immunol. Rev., 1998, Vol.162, pp. 77-87.	
	6	HARRIS R.S., et al., "AID Is Essential for Immunoglobulin V Gene Conversion in a Cultured B Cell Line"; Curr. Biol., 2002, Vol. 12, pp. 435-8.	
	7	KINOSHITA K. et al., "Linking class-switch recombination with somatic hypermutation"; Nat. Rev. Mol. Cell Biol., 2001, Vol. 2, pp. 493-503.	
	8	KOBRIN B.J. et al., "The Somatic Instability of Immunoglobulin Genes in Cultured Cells"; PP. 11-28 (Chapter 2) in Somatic hypermutation in V regions (ed. Steele, E. J.), CRC Press, Boca Raton, Florida, 1990.	
	9	KUPPERS R. et al., "Mechanisms of chromosomal translocations in B cell lymphomas"; Oncogene, 2001, Vol. 20, No. 40, pp. 5580-94.	
↓	10	LIN M.M. et al., "Sequence dependent hypermutation of the immunoglobulin heavy chain in cultured B cells"; Proc. Natl. Acad. Sci. USA, 1997, Vol. 94, No. 10, pp. 5284-9.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	10/501,628
				Filing Date (I.A. Filing Date)	01/15/2003
				First Named Inventor	Alberto Martin
				Art Unit	to be assigned
				Examiner Name	to be assigned
Sheet	2	of	4	Attorney Docket Number	96700/905

NON PATENT LITERATURE DOCUMENTS				
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.		T ²
	11	LIN M.M. et al., "The effects of E-mu, 3'-alpha (hs 1,2) and 3'-kappa enhancers on mutation of an Ig-VDJ-C-gamma-2a Ig immunoglobulin heavy gene in cultured B cells"; Internatl. Immunol., 1998, Vol.10, No. 8, pp. 1121-1129.		
	12	MARTIN A. et al., "AID and mismatch repair in antibody diversification"; Nat. Rev. Immunol., 2002, Vol. 2, No. 8, pp. 605-14.		
/KM/	13	MARTIN A. et al., "Somatic hypermutation of the AID transgene in B and non-B cells"; Proc. Natl. Acad. Sci. USA, 2002, Vol. 99, No. 19, pp. 12304-08.		
	14	MARTIN A. et al., "Activation-induced cytidine deaminase turns on somatic hypermutation in hybridomas"; Nature, 2002, Vol. 415, pp. 802-6.		
	15	MURAMATSU M. et al., "Class Switch Recombination and Hypermutation Require Activation-Induced Cytidine Deaminase (AID), a Potential RNA Editing Enzyme"; Cell. 2000, Vol. 102, pp. 553-63.		
	16	MUSCHEN M. et al., "Somatic Mutation of the CD95 Gene in Human B Cells as a Side-Effect of the Germinal Center Reaction"; J. Exp. Med., 2000, Vol.192, No. 12, pp. 1833-39.		
	17	OKAZAKI I. et al., "The AID enzyme induces class switch recombination in fibroblasts"; Nature, 2002, Vol. 416, pp. 340-45.		
	18	PASQUALUCCI L. et al., "BCL-6 mutations in normal germinal center B cells: Evidence of somatic hypermutation acting outside Ig loci"; Proc. Natl. Acad. Sci. USA, 1998, Vol. 95, No. 20, pp. 11816-21.		
	19	PASQUALUCCI L. et al., "Hypermutation of multiple proto-oncogenes in B-cell diffuse large-cell lymphomas"; Nature, 2001, Vol. 412, pp. 341-6.		
	20	PETERS A. et al., "Somatic Hypermutation of Immunoglobulin Genes Is Linked to Transcription Initiation"; Immunity, 1996, Vol. 4, pp. 57-65.		

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)		Complete if Known			
		Application Number	10/501,628		
		Filing Date (I.A. Filing Date)	01/15/2003		
		First Named Inventor	Alberto Martin		
		Art Unit	to be assigned		
		Examiner Name	to be assigned		
Sheet	3	of	4	Attorney Docket Number	96700/905

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
/KM/	21	PETERSEN-MART S. K. et al., "AID mutates E. coli suggesting a DNA deamination mechanism for antibody diversification"; Nature, 2002, Vol. 418, pp. 99-104.	
	22	POLTORATSKY V. et al., "Error-prone Candidates Vie for Somatic Mutation"; J. Exp. Med., 2001, Vol. 192, No. 10, pp. F27-F30.	
	23	RADA C. et al., "The intrinsic hypermutability of antibody heavy and light chain genes decays exponentially"; EMBO J., 2001, Vol. 20, No. 16, pp. 4570-6.	
	24	REVV P. et al., "Activation-Induced Cytidine Deaminase (AID) Deficiency Causes the Autosomal Recessive Form of the Hyper-IgM Syndrome (HIGM2)"; Cell, 2000, Vol. 102, No. 5, pp. 565-75.	
	25	SALE J.E., et al., "TdT-Accessible Beaks Are Scattered over the Immunoglobulin V Domain in a Constitutively Hypermutating B Cell Line"; Immunity, 1998, Vol. 9, No. 6, pp. 859-69.	
	26	SHEN H.M. et al., "Mutation of BCL-6 Gene in Normal B Cells by the Process of Somatic Hypermutation of Ig Genes"; Science, 1998, Vol. 280, pp.1750-52.	
	27	SHEN H.M. et al., "The TATA binding protein, c-Myc and survivin genes are not somatically hypermutated, while Ig and BCL6 genes are hypermutated in human memory B cells"; Intl. Immunol., 2000, Vol. 12, No. 7, pp. 1085-93.	
	28	SPENCER J. et al., "Characteristics of Sequences Around Individual Nucleotide Substitutions in IgV-H Genes Suggest Different GC and AT Mutators"; J. Immunol., 1999, Vol.162, No. 11, pp. 6596-601.	
	29	TUMAS-BRUNDAGE K. et al., "The Transcriptional Promoter Regulates Hypermutation of the Antibody Heavy Chain Locus"; J. Exp. Med., 1997, Vol. 185, No. 2, pp. 239-50.	
↓	30	YELAMOS J. et al., "Targeting of non-Ig sequences in place of the V segment by somatic hypermutation"; Nature, 1995, Vol. 376, No. 6537, pp. 225-29.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>		Complete if Known			
		Application Number	10/501,628		
		Filing Date (I.A. Filing Date)	01/15/2003		
		First Named Inventor	Alberto Martin		
		Art Unit	to be assigned		
		Examiner Name	to be assigned		
Sheet	4	of	4	Attorney Docket Number	96700/905

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
/KM/	31	YOSHIKAWA K. et al., "AID Enzyme-Induced Hypermutation in an Actively Transcribed Gene in Fibroblasts"; Science, 2002, Vol. 296, No. 5574, pp. 2033-6.	
/KM/	32	ZAN H. et al., "Induction of Ig Somatic Hypermutation and Class Switching in a Human Monoclonal IgM+ IgD+ B Cell Line In Vitro: Definition of the Requirements and Modalities of Hypermutation" J. Immunol., 1999, Vol. 162, No. 6, pp. 3437-47.	
/KM/	33	ZAN H. et al., "B Cell Receptor Engagement and T Cell Contact Induce bcl-6 Somatic Hypermutation in Human B Cells: Identity with Ig Hypermutation"; J. Immunol., 2000, Vol. 165, No. 2, pp. 830-9.	
/KM/	34	ZHANG W. et al., "Clonal instability of V region hypermutation in the Ramos Burkitt's lymphoma cell line"; Intl. Immunol., 2001, Vol. 13, No. 9, pp. 1175-84.	

Examiner Signature	/Kimberly Makar/	Date Considered	08/20/2007
--------------------	------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.